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ORIGINAL ARTICLE

A point score system for allocating cadaveric kidneys for transplantation based on patient age, waiting time and HLA match

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Abstract

A revised allocation system for cadaveric kidney donations was introduced in Hong Kong in July 1996 to take into consideration the age and waiting time of patients on the waiting list for transplantation, and the degree of HLA mismatch of the potential donor against the waiting patients. In recognition of the established benefits of transplanting donor kidneys with zero mismatched antigens against the recipient, the revised system provided that cadaveric kidneys would be transplanted whenever possible to patients against whom the donor had zero mismatched antigens. A total of 168 kidneys were allocated over a 45-month period using the revised system. The 3-year actuarial graft survival was 83%, which exceeded the figure reported for the same population 3 years previously. It is concluded that the revised system is fulfilling its desired objective to remove some older, long-term patients from the waiting list but that additional follow-up is required.

Key words: Allocation, HLA, Point score

中文摘要

在1996年7月，香港引進了一個經修訂的屍腎分配系統，其中考慮了輪候屍腎病人的年齡、等候時間及人類白細胞抗原的失配程度。因為沒有抗原失配的腎臟移植結果較為理想，此修訂的系統盡量將屍腎分配給零抗原失配的病人。在採用了此修訂系統的45個月內，共分配了168個腎臟，3年的實際器官存活率為83%，比以往的數字為高。總結而言，本修訂系統達到了其理想的目的，能把年齡較高及接受透析診療較長的病人辟除屍腎等候者名單，可是仍需等待較長追縱期的結果。

INTRODUCTION

The difficulty of obtaining cadaveric organ donors in Asian societies is well known. At any one time in Hong Kong, approximately 1000 patients are on the waiting list for cadaveric renal transplantation. As of 30 June 2000, 1022 patients were on the waiting list. In the 10 years from 1 January 1990 to 31 December 1999, an average of only 40 cadaveric kidneys were transplanted each year (range 31 to 58 per year). This major imbalance between the number of patients on the waiting list and the number of kidneys available results in considerable difficulty in achieving a fair and equitable allocation of cadaveric organs. To overcome this problem, we have introduced a point score allocation system to take account of the patient's age, length of time on the waiting list, and HLA match with the donor. This paper documents our experience with the revised point score system between July 1996 and April 2000.

PATIENTS AND METHODS

During the period from 1 July 1996 to 30 April 2000, a total of 168 cadaveric kidneys were available for transplantation in Hong Kong. The kidneys were allocated to 78 male recipients and 90 females. The recipients had been on the waiting list for cadaveric transplantation for periods ranging from 8 to 255 months (mean 93.5; median 79.5). Follow-up time after transplantation ranged from 1 to 44 months (mean 19.4; median 20). Of the patients, 146 were followed for at least 6 months. All donors were typed for HLA-A, -B,

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and -DR antigens in the Tissue Typing Laboratory at Queen Mary Hospital as part of the pretransplant work-up that forms the standard procedure throughout the SAR.

Wherever possible, kidneys were allocated to waiting patients against whom the donor had no incompatible antigens at either the HLA-A, -B, or -DR loci. If no patients with a zero-antigen mismatch were identified, kidneys were allocated according to a point score calculated for each ABO blood group compatible patient on the waiting list of the hospital cluster in which the donor was identified. For the purposes of this calculation, potential recipients were separated into four hospital clusters corresponding to whether they were normally treated in hospitals or dialysis units affiliated with Queen Mary Hospital, Prince of Wales Hospital, Princess Margaret Hospital or Queen Elizabeth Hospital.

Point scores were allocated according to the following formula:

Point score = (60 - age of patient) + (years on waiting list x 5) + (10 for patients below 15 years of age) + (HLA score)

The HLA score was awarded as follows on the basis of the number of HLA antigens in the potential donor that were mismatched against the potential recipient:

20 if HLA-B and HLA-DR mismatch = 0
15 if HLA-B and HLA-DR mismatch = 1
10 if HLA-B and HLA-DR mismatch = 2
plus 5 extra if HLA mismatch = 0

As far as possible, kidneys were allocated to the patients with the highest point score in the hospital cluster in which the donor was identified. Regardless of point score, however, patients were excluded from transplant if any of the following conditions applied:-

1. The lymphocytotoxicity crossmatch against the cadaveric donor was positive;
2. The patient had a current or previous history of antibodies against incompatible HLA antigens present in the donor;
3. The present donor shared an incompatible antigen against the patient with a donor from a previous failed transplant; and
4. Other clinical or social contraindications to transplant were present.

RESULTS

The distribution of mismatched donor antigens in the 168 recipients is shown in figure 1. It may be seen that

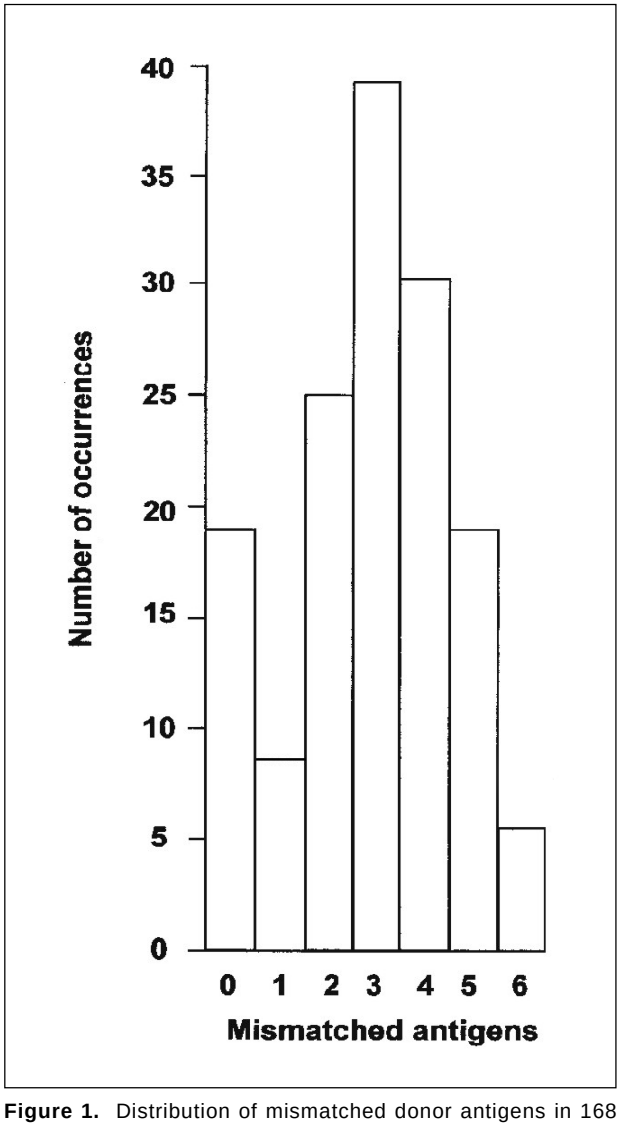

Figure 1. Distribution of mismatched donor antigens in 168 cadaveric renal transplants.

18 kidneys were allocated to recipients for whom the donor had no mismatched HLA antigens against the recipient. The age distribution is shown in figure 2. The recipient ages ranged from 8 to 60 years (mean 41.2; median 42). The outcome of 146 recipients with at least 6 months post-transplant follow-up is shown in table 1. The actuarial graft outcome of all 168 recipients is shown in figure 3. The cause of death listed on the Hospital Authority Transplant Registry is shown in table 2 for 16 patients who died at some stage after transplantation. In only one of these cases was rejection listed as a contributory cause of death. The patient survival time following transplantation in the 16 patients who died ranged from 0 to 34 months (median 4 months).

DISCUSSION

Before 1994, cadaveric kidneys in Hong Kong were allocated predominantly on the basis of the number of

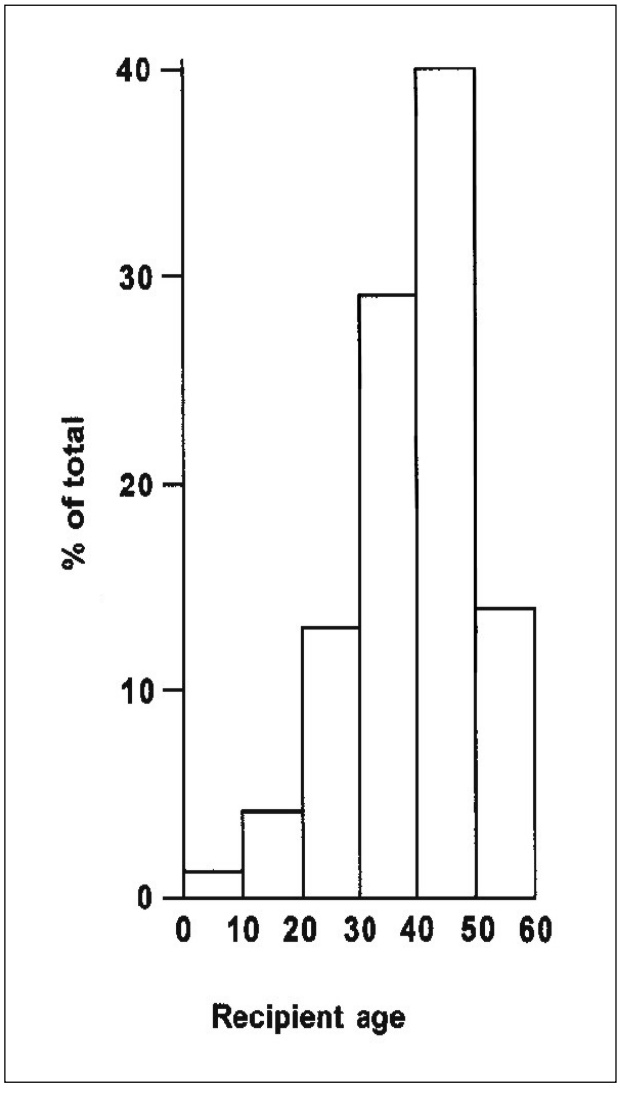

Figure 2. Age distribution of recipients of 168 cadaveric renal transplants.

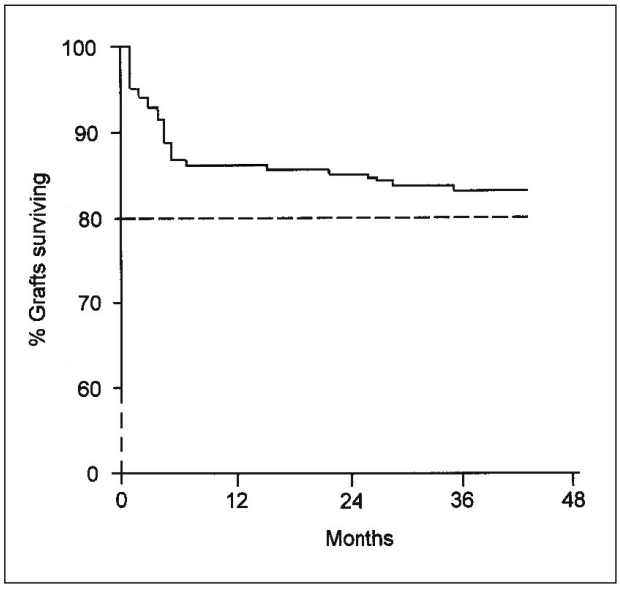

Figure 3. Actuarial graft survival of 168 cadaveric renal transplants.

Table 1. Outcome of 146 cadaveric transplants with at least 6 months follow-up.

Outcome	Number	%
Alive with functioning graft	114	78.1
Alive after graft failure	13	8.9
Deceased	16	11.0
No information	3	2.0
Total	146	100.0

Table 2. Cause of death in 16 patients who died after transplantation.

Cause	Number
Lung infection	4
Cardiac arrest	3
Malignancy	2
Liver failure	1
CVA	1
Septicemia	2
Others	3

HLA antigens in common between the donor and patients on the waiting list. As far as possible, kidneys would be allocated to patients with the most antigens in common with the donor. The number of HLA antigens in common, based on a typical typing for HLA-A, HLA-B and HLA-DR, could range from six to zero. Since for any particular donor there would invariably be many recipients with the same number of antigens in common, a secondary method of selection was necessary. This method varied from one hospital to another and included such criteria as age (younger recipients were preferred), period of time on the waiting list, clinical considerations, psychosocial considerations, etc.

There was, therefore, some recognition that certain patients may be more appropriate recipients than others of a particular donated kidney. A 21-year-old patient, for example, may be more appropriate as a recipient than a 59-year-old because the younger patient would be expected to live longer and therefore keep the kidney longer. Alternatively, a 55-year-old who has been on the waiting list for 15 years may be suffering more complications from prolonged dialysis than a younger patient and may be causing an excessive drain on expensive resources. Transplantation of this patient may not only improve the patient's quality of life but could also result in a significant saving of resources.

Despite the recognition that age and waiting time were important considerations in the allocation of cadaveric

kidneys, there was no unified system in place in the territory to account for these factors prior to 1994. In 1994, the Central Renal Committee introduced a point score allocation system to standardize the weighting of age and waiting time.

Under the 1994 system, a point score was calculated as follows:
Point score = (60 - age of patient) + (years on waiting list x 3) + (5 for patients aged below 13 years of age)

Having ranked potential recipients in terms of the number of HLA antigens in common with the donor, the point score would be used to determine the ranking of patients amongst those with the best HLA match.

The formula was devised empirically and was selected from a number of models giving different weightings to age and waiting time. It was also recognized that pediatric and prepubertal patients have additional needs, and an additional weighting for these patients was included in the formula. Applying the formula to typical patients, a 24-year-old patient who had been on the waiting list for 4 years would qualify for 48 points, for example, while a 56-year-old who had been on the waiting list for 15 years would qualify for 49 points. This system remained in operation on an experimental basis for approximately 2 years.

During the trial period, there became increasing awareness that allocation of kidneys strictly on the basis of antigens in common with the donor has some fundamental disadvantages. In particular, a potential recipient with one or more uncommon HLA antigens is unlikely to find a matched donor and will remain on the waiting list for a long period. The concept of *mismatched* antigens in the donor helps overcome this disadvantage and more closely reflects the biological factors that determine why a particular donor may be more suitable or less suitable for a particular patient.

In terms of predicting possible graft rejection, it is important to know what is present in the donor that is not present in the recipient since it is this that ultimately results in rejection of the transplanted organ. Various examples to illustrate this concept are depicted in table 3, using data from a hypothetical donor and five hypothetical patients. The donor has only DR15 detectable at the HLA-DR locus. This means, in all probability, that the donor has inherited DR15 from both of his parents and is therefore homozygous for DR15. The same applies to patient 1 and patient 4.

Patient 1 has the same phenotype as the donor and therefore has five antigens in common with the donor. Conversely, the donor may be considered to have zero antigens mismatched against the patient.

Comparing the donor with patient 2, it may be seen that the donor has HLA-A11, which is not present in the patient. The other antigens in the donor are also present in the patient. The donor therefore has one incompatible antigen (HLA-A11) against the patient. If a kidney from this donor were to be transplanted to patient 2, the incompatibility could ultimately lead to an immune response by the recipient against the donated organ. The fact that patient 2 has HLA-DR7, which is not present in the donor, is of no relevance because the donor's immune system will be unaffected by the DR7 in the patient. Conversely, the fact that the patient has two HLA-DR antigens identifiable while the donor has only one is not relevant because it assumed that the donor had only HLA-DR15 present, which will not result in an immunological reaction by the recipient.

In the case of patient 5, it may be seen that the donor has three antigens mismatched against the patient: A2, A11, and B13. On balance, this patient would be expected to have a greater risk of rejecting an organ from that donor than would patient 2 because the level of mismatch is higher.

In recognition of these considerations, and to fine-tune the other weightings based on 2 years of experience, the Central Renal Committee revised the allocation system in 1996 to include a component representing the number of mismatched HLA antigens in the donor. An additional feature of the revised allocation system was that kidneys

Table 3. Antigens in common versus antigens mismatched.

		Antigens in common	Antigens mismatched
Donor	HLA A2, A11, B13, B75, DR15		
Patient 1	HLA A2, A11, B13, B75, DR15	5	0
Patient 2	HLA A2, A33, B13, B75, DR15, DR7	4	1
Patient 3	HLA A2, B13, B46, DR15, DR9	3	2
Patient 4	HLA A24, A33, B13, B75, DR15	3	2
Patient 5	HLA A26, A33, B60, B75, DR15, DR4	2	3

would be transferred out of the hospital cluster in which the donor was identified if there was a patient in another cluster against whom the donor had zero mismatched HLA antigens. This decision reflected the well-recognized benefits of transplanting zero mismatch kidneys and followed the practice that had been in operation in USA, Europe and Australasia for several years.

The major departure from previous practice in Hong Kong was the use of HLA matching as a *contributory* factor in the allocation of kidneys rather than as the primary determining factor. The score attributed to the degree of HLA mismatching was calculated to reflect the well known phenomenon that mismatches for HLA-B and -DR have a greater impact on graft outcome than mismatches for HLA-A. The distribution of the number of mismatched HLA antigens in the donors following the introduction of the revised system (Fig. 1) is consistent with there having been no special selection for the number of mismatches once the recipients with zero mismatched antigens in the donor had been chosen. Leaving aside the 18 patients with zero mismatches, the distribution of the number of mismatched HLA antigens in the donors showed a random distribution with 48.6% having three mismatches or less and 51.4% with four mismatches or more.

The revised allocation system apparently achieved its aim to clear some of the older patients from the waiting list. As shown in figure 2, 53% of recipients were above the age of 40 years and 13% above 50 years. This is a significant departure from the previous preference for transplanting younger patients.

In order to evaluate the revised system fully, it is necessary to determine whether there was any significant change in the outcome of transplantation after the revised system was introduced. The Kaplan Meier analysis shown in figure 3 shows the typical pattern of accelerated graft loss during the first 6 months followed by a leveling off and only minimal graft loss thereafter. Graft survival at the end of 3 years was 83%. Previously we have reported on the outcome of 352 cadaveric kidney transplants performed over a 25-year period in Hong Kong and reported a 3-year actuarial graft survival of 76% (1). Hence, it is apparent that the revised allocation system is not resulting in a worse outcome than was obtained previously. A point of some concern is that 16 recipients died after transplantation (Table 1). In only one case was rejection given as a contributory cause of death. However, it is noteworthy that eight of the 16 patients died within 4 months of transplantation and it is difficult without further information to exclude a relationship between these deaths and the preceding transplants.

Of the 18 patients who received kidneys with zero antigen mismatches, one (5.6%) died after transplantation. By convention, death after transplantation is regarded as graft failure, even if the patient was known to have a functioning graft at the time of death. Among the 150 patients who received a kidney with one or more antigens mismatched there were 28 failures (13 patients surviving and 16 deaths). This failure rate is not statistically significant from that of the zero antigen mismatched kidneys ($x^2 = 1.6$; $p < 0.2$).

CONCLUSION

The point score system introduced in 1996 appears to be achieving its aim of providing a fair and more equitable method of allocating cadaveric kidneys than that which existed previously. The system is reproducible and provides an accountable basis for allocation. There appears to have been an increase in the number of older and long-term patients receiving transplants than was observed previously. Significantly, 50% of the patients transplanted had been on the waiting list for more than 6 years, the longest for over 21 years. In this respect the new system must be considered successful.

Less impressively, it was noted that 9.5% of the transplanted patients died within 34 months of the transplant and that half of the deaths occurred within 4 months of the transplant. It will be necessary to monitor this matter carefully over the next few years.

Under the new allocation system, less emphasis than previously has been placed on HLA matching other than to encourage the transplantation of patients against whom the donors have no incompatible antigens. This does not appear to have affected the overall outcome, and the observed successful outcome of 83% at 3 years exceeds the figure observed in the territory in a previous report. There was no significant difference in the failure rate of kidneys with zero mismatched antigens compared with those with non-zero mismatches. This is not necessarily of relevance, however, because it is well known that much of the benefit of HLA matching is in long-term rather than short-term outcome. Extended follow-up over many years will be necessary to appreciate the full benefits of the revised system.

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